

## **REMARKS**

### **Claim Amendments**

The clarity issues with respect to the definition of X are resolved. The two methyl groups in the compound of formula I attached to X are removed, as the substituents are already defined in the definition of X. Support for this amendment can also be found, for example, in the species depicted on pages 8-14 of the specification.

The definition of Z is amended. Previously the definition recited that C atoms in the C<sub>1</sub> to C<sub>5</sub> alkyl are optionally substituted by O or S. The term “substituted” is changed to “replaced.” It is clear from compounds 10, 11 and 12 depicted on pages 11 and 12, that the term “replaced” was intended.

The definition of Z is further amended by reciting that the structure depicted for Z “is bound by an ethylene or a methylene bridge to R<sub>5</sub>.” Support for this amendment can be found, for example in the compounds of claims 18-21 and 24.

The definition of R<sub>5</sub> is also amended in claim 1, to include COOH and NH<sub>2</sub>. Support for this amendment can be found, for example, on page 7, third full paragraph.

The definitions of R<sub>6</sub> and R<sub>7</sub> are also clarified by reciting that these two groups can be connected together by a C<sub>3</sub>-alkylene group to form a cyclohexyl.

Other amendments to the form of the claims were also made whereby the rejections to the form of the claims are moot. Support for this amendment can be found, for example in the compounds of claims 18-21 and 24.

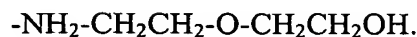
Withdrawn claims directed to conjugates are cancelled without prejudice or disclaimer

### **The Rejections Under 35 USC 103**

Applicants respectfully disagree with the rejection. The Office Action combines 8 references, takes parts of various compounds from different references and combines them to yield applicant's claimed compounds.

Such combination of various parts of different compounds is not a proper basis for an obviousness rejection under strong Federal Circuit precedent such as under *In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992) and *In re Baird*, 16 F.2d 380, 29 U.S.P.Q. 2d 1550 (Fed. Cir. 1994).

Note in this regard, particularly, the analysis used by the Court in *Jones*. The group at issue in *Jones* had the structure



The PTO tried to rely on the single reference's compound having two  $\text{CH}_2\text{CH}_2\text{OH}$  groups attached to a single N atom, instead of linked together as shown above. The Court stated that one could not ignore the fact that the two  $\text{CH}_2\text{CH}_2\text{OH}$  groups were not joined together to form the ether linkage-containing group required in the claim. One could not simply rely on the "- $\text{CH}_2\text{CH}_2\text{O}$ -" features of the reference; one had to consider the entirety of the structure involved. The Patent and Trademark Office also tried to rely on a morpholino group in the single reference wherein the nitrogen atom has two ethyl groups bonded to it and linked to each other by a single oxygen atom, thereby allegedly providing the "missing" ether oxygen noted above. Again, the Court stated that one could not ignore the entirety of the structure, i.e., the fact that this prior art group compound was cyclic. One could not apply components of its structural features in isolation apart from the group's overall structure. Other similar analyses were rejected by the Court.

Likewise here, the teaching of WO '810 that an increase in the number of sulfonic acid groups resulted in a reduction of toxicity cannot be separated from the specific compounds taught by WO '810. Analogously, the teaching in Chorev that maleimido forms a stable thio-ether bond cannot be separated from the specific compounds taught by Chorev. Such piecing together of an invention from various differing structures from different references is improper under well settled precedents.

Thus, a teaching that a certain substituent for a certain disclosed compound lowers its toxicity, and a further teaching that another substituent on a different compound renders such compound more stable, and so on, do not create motivation to employ these substituent on any position of any other particular compound. Disclosure of particular generic formulae and/or species with their particular set of structural components, under *Baird* and *Jones*, do not motivate one of ordinary skill in the art to select various structural features from different compounds in isolation and apply them to other compounds.

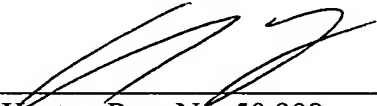
Additionally, applicants submit that without applicants' own disclosure as a roadmap to piecing together the claimed invention herein, one of ordinary skill in the art would not have

ended up with applicants' invention based on the disclosure of the various references. For example, not one single reference even generically teaches each and every component of applicants' claimed invention. Moreover, there is not motivation in the references for the particular combinations alleged. For example, the compounds of WO '810 and Chorev have nothing to do with each other. Why would one of ordinary skill in the art select various unrelated compounds for combining them together?

For all the foregoing reasons, the claims are not obvious. Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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